DIAGNOSIS OF TUBERCULOSIS APART FROM PHYSICAL SIGNS.

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So far as I am able to ascertain, the first aid in this direction was the discovery of the bacillus of tuberculosis by Koch, which was published in March, 1882, at a meeting of the Physiological Society of Berlin. At the same time, satisfactory experimental evidence was presented as to its etiological relation to tuberculosis in man and in susceptible lower animals, and its principal biological characters were given. This achievement, the result of patient and intelligent scientific investigation will always rank as one of the most important in the history of medicine.

The previous demonstration by Villerman in 1865, confirmed by Coenheim in 1877, and by others, that tuberculosis might be induced in healthy animals by inoculation of tuberculosis material, paved the way to his great discovery, and advanced pathologists were quite ready to accept that view. The more conservative have since been obliged to yield to the experimental evidence which has received confirmation in all parts of the world.

THE DETECTION OF THE TUBERCLE BACILLUS.

My first thought on this part of the subject was that it would be superfluous to go into detail in the methods of detecting the tubercle bacillus, as I feel that every one is quite familiar with this part of the diagnosis. However, a few lines may not be out of order.

Detection of the bacilli in the sputum. This will be referred to only in connection with the body exudate. By the exudates, we mean contents of any of the serous cavities, cerebro-spinal and the exudates from the genito-urinary tract, sinuses, etc.

In any exudate where the bacilli are suspected and are too scarce to be found by simply making a smear in the usual manner, then the exudate should be centrifugalized and a smear made of the sediment. If the smear does not then show bacilli, then the sediment may be digested and centrifugalized again, and other smears made and examined. Should this fail, the sediment should be injected into some of the susceptable lower animals, such as the rabbit or guinea pig. In the course of a few weeks if the animal does not die, it should be killed and the different organs of the body examined both in the gross and microscopic specimen.

In the case of localized lesions, such as lymph glands, the suspected gland should be removed, sections made, and some examined for actual tubercles and others stained and examined for the tubercle bacilli.

The detection of elactic tissue in the sputum can in the majority of cases be said to come from a lung, the seat of a tubercular involvement, provided, however, external sources can be excluded, such as may accidentally gain entrance to the sputum by the ingestion of meat. If the latter is suspected, then the patient should be placed on a milk diet for some days and the sputum again examined. It should be borne in mind that tuberculosis is not the only pathological condition which will cause elastic tissue to appear in the sputum.

Soon after the discovery of the tubercle bacillus by Koch, he discovered a toxic substance in cultures of tubercle bacilli which is soluble in glycerine, and which in very minute doses produces a febrile reaction and other decided symptoms when injected subcutaneously into tuberculous animals. This discovery must rank as one of the first in importance in scientific medicine.

This substance is now generally known under the name of tuberculin. It is soluble in water, insoluble in alcohol, passes readily through a dialyzable membrane, and is not destroyed by boiling temperature. A number of modifications of Koch's original tuberculin are now on the market. In 1892 Tozzoni and Cattoni presented some experimental evidence which indicated that injections of Koch's original tuberculin into guinea pigs produced in these animals a certain degree of immunity against tuberculosis and that this immunity depends upon the presence of an antituberculin formed in the body of a partially immune animal.

Numerous experiments by veterinary surgeons made on tuberculous cows have shown that the injection of Koch's tuberculin in these animals in doses of from 30 to 40 centigrams produces a rise in temperature of one to three degrees C. The febrile reaction usually occurred in from twelve to fifteen hours after the injection. In non-tuberculous animals no reaction was noted, and the experiments made justified the suspicion that tuberculosis exists if an elevation in temperature of a degree or more occurs as a result of the subcutaneous injection of the dose mentioned.

It might not be out of order to mention here that a step in the direction of this form of diagnosis was the discovery by Sir A. E. Wright, of London, when he discovered the method of determining the much mooted question, "the opsonic index." Just how much value we can place on this method of diagnosis of tuberculosis has not yet been decided to the satisfaction of all the medical profession. However, from a review of the literature, in spite of all the contradictory statements both for and against this method, it would seem that the greater per cent. of patients suffering from active lesion of tuberculosis show a constantly fluctuating index to the tubercle bacilli. This statement is based entirely upon literature obtained from the journals as a result of observations claimed by different workers. I have no personal experience with the tuberculo-opsonic index.

A study of the tuberculo-opsonic index shows that there is a large percentage of fluctuating indices in the cases of advanced diseases. It is also interesting to note that the percentage of variations of the opsonic index from the normal is about the same as the percentage of positive reactions to the tuberculin tests in the less advanced cases and is greater in the more advanced cases.

Later in 1907, Calmette of Lily, France, described the reaction which now bears his name, "Calmette reaction," "Opthalmo-tuberculin reaction," "conjunctival reaction." Calmette in his original article recommended the use of the precipitated or purified tuberculin, which may be obtained in the powder, tablet, or liquid form, ready for use. The tablets are used as follows: One tablet added to one CC. of .85% salt solution makes a one per cent solution, which thus made is perfectly clear.

APPLICATION OF THE TEST.

The conjunctiva of both eyes are examined, and any injection of the vessels noted. The solution is warmed and one drop instilled into the eye, holding the lower lid out from the eye-ball and allowing the drop to spread over the conjunctival sack by gentle manipulation of the lower lid before allowing the lid to be closed.

OBSERVATION OF THE REACTION.

Much description has been given in this connection. After summing up the whole thing the chief point is, whether there is or is not a positive reaction. The reaction varies from a mild to a severe grade of conjunctivitis, reaches its maximum in about 24 to 36 hours, and subsides in from about 48 hours to one week. As in any catarrhal conjunctivitis there is a bright brick-red conjunctival injection in the coarse meshes of the blood vessels, most pronounced in the fornix and towards the inner canthus and fading toward the cornea.

In the meshes of the injected vessels the conjunctiva is ecchymotic; the caruncle is hypermic and edematous; there is edema of the lids, especially the lower lid, so that in the more severe reactions there is a narrowing of the palpebral aperture. There is usually an increased lacrymation, and in the more severe reactions a mucous, or muco purulent, secretion which accumulating during the night may close the lids. There is no subjective symptom in the mild grades, but in the more marked reactions there is a sensation of a foreign body in the eye and a burning and smarting with photobia.

The strength of the tuberculin is claimed to have much to do with the reaction. A .5 per cent. solution for children and 1 per cent. solution for adults will give a typical conjunctival reaction. The Germans have used as high as a 4 per cent. solution, the French and Americans from .5 per cent. to 1 per cent. of the dried tuberculin which had been precipitated by alcohol. In spite of the varying strength used the reaction has varied but very little on the whole. Repeated instillations have given positive results in non-tubercular patients where increasing strengths have been used.

THE VON PIRQUET TUBERCULIN TEST.

Two solutions are necessary; a 25 per cent. solution of Koch's old tuberculin, consisting of one part of T. O., one part of carbolic acid in glycerine and two parts of .85 per cent. sterile salt solution; and a blank solution consisting of one part 5 per cent. carbolic acid in glycerine and three parts sterile .85 per cent. salt solution.

To preserve the two solutions in a sterile manner without evaporation and to have a definite amount for each test, a measured drop is drawn into a capillary tubing and sealed.

The scarifier may be metal or glass, should not be sharp enough to break the skin, and it should be a flat-sided tip, about 1-16 inch diameter. The edge is used in scarifying.

APPLICATION OF THE TEST.

A small area of skin on the inner surface of the forearm or over the insertion of the deltoid is cleansed with ether. Break off both ends of all three capillary tubes, two containing the 25 per cent. tuberculin and one the blank solution, blow two drops of tuberculin on the arm about one and one half inches apart and one drop of blank solution between the two drops of tuberculin, dip the scarifier in ether, dry and revolve the edge of the tip about four times in the tuberculin, holding the scarifier at right angles to the skin surface, using enough pressure to make a slight dent in the skin. The same procedure is carried out in the other two drops. The only immediate result will be a slight depression in the skin. Allow the drop to dry thoroughly.

REACTION.

Usually at the end of twenty to twenty-four hours, the reaction, if any occurs, is at its maximum. A typical reaction consists of hyperemic indurated swelling, rather sharply circumscribed about one cm. in diameter with a deeper colored pin-head sized central depression. The blank shows nothing, or rarely a dull red point. Occasionally a more marked tuberculin reaction results, that is vesicle formation in the center, a hyperemic swelling of twice the usual size, and finally crust formation. The reaction subsides in from one to four weeks by gradual diminution of the hyperemia, and induration, if the reaction be of a mild grade, and by disquamation if the reaction be of severe grade.

No constitutional symptoms have ever been noted. The only subjective symptoms are a slight grade of itching and some tenderness if the reaction is severe.

CONCLUSIONS.

The per centage claimed for the Von Perquet test, the conjunctival test and the tuberculo-opsonic tests are substantially the same, ranging from 85 per cent. to 95 per cent. in the favorable cases and from 30 per cent. to 40 per cent. in the advanced unfavorable cases. The more advanced the disease, the smaller the number of positive reactions.

The intensity of the reaction does not consistently follow any rule, but tends to be greater in less advanced cases of the disease.

SUBCUTANEOUS ADMINISTRATION.

Swanson Brown recommends the use of Koch's old tuberculin, while others recommend the use of some of the modifications of Koch's old tuberculin. The chief point of difference, if any, is the proper dose of whatever preparation is used.

DOSAGE.

1-10 mg. for an adult should be the initial dose. If a reaction is not obtained, then the dose should be repeated on the third day after the first dose, but the dose should be gradually increased up to .8 to 1 mg. Some advise a single large dose, fearing the continued small doses will confer a certain amount of immunity on the patient.

ADMINISTRATION.

The subscapular region is to be chosen. In order to arrive at any given amount to be used for a dose the tuberculin must be diluted, preferably by the physician. This is best done by means of a pipette graduated to read hundredths of a cubic centimeter and a graduated cylinder. A solution of .25 per cent. phenol in a physiological salt solution is probably the best diluent. Solutions should be made fresh for injections. The phenol solution may be kept several days in a colored bottle.

Many workers prefer to administer the tuberculin in the afternoon. The patient should be kept quiet the day of the injection, not necessarily in bed. The object of rest is to avoid every possible cause that may influence the reaction. The temperature should be recorded for two or three days before, during the reaction, and after the reaction.

CONTRA INDICATIONS.

Tuberculin should not be administered when a patient's oral temperature is 100 F. at any time of day (Koch). Others claim this rise of temperature is not an objection. It would seem to me that it is.

In patients with excessive physical signs it should be used with caution. Night sweats, great dysponea, recent hemoptasis, general glandular involvement, heart or renal disease, epilepsy are all said to be contra-indications. It should never be used after an acute disease nor for three weeks after a febrile period of unknown cause. In some neurasthenic patients the insertion of the needle alone will cause a rise of temperature. In such cases a hypodermic of sterile water should be the preliminary treatment.

REACTION.

In a typical tuberculin reaction the patient begins to feel indisposed about eighteen hours after the injection. This becomes more marked and he is willing to go to bed or remain in bed. Severe headache, general malaise, pain in the back and limbs, a slight tendency to cough, loss of desire for food, in some cases nausea and vomiting, and in some cases great prostration, temperature often reaches 101, usually 100, and may go as high as 107 without apparent ill results. There may be a change in the physical signs in the chest. Absence of this change in the chest is not proof that a reaction has not occurred. When changes do occur, they are such as are produced by hyperemia in the tuberculous area, rough breathing, waivy inspiration, crepitis, possibly a slightly percussion note. There may be herpes labialis during prolonged and severe reactions; swelling, redness and pain at point of injection vary greatly. Other symptoms more or less constant are faintness, giddiness, insomnia, somnolence, fatigue, restlessness, weakness and localizing symptoms, oppression in the chest, increased expectoration, dysponia, pleurisy. Other foci of tuberculosis may be discovered by localizing symptoms in joints, glands, bones and bladder. A number of blood changes have been described.

RESULTS AND STATISTICS.

Specificity. Does the reaction occur in diseases other than tuberculosis? It is claimed by many that it does. So far as I am able to ascertain these claims have not been based on post-mortem findings. Without post mortem findings these statements are of little value, as there may be tubercular lesions apart from those suspected that are capable of giving a positive reaction. For instance, a sound lung may be suspected, and no physical signs ever develop, and still a reaction be obtained as a result of a lesion in the retro-peritoneal glands.

Does it fail to occur in known cases of tuberculosis? There is good evidence that it does. Healed or particularly incapsulated lesions are said not to react. In advanced cases with the bacilli in the sputum it is said not to react. I have been unable to find a report of a single case of early or incipient tuberculosis where the dose of 1-100 cc. old tuberculin has failed to react.

After a careful review of the literature on this subject anything like accurate statistics are very indefinite. Notwithstanding the varied reports and contradictory evidence, I feel quite certain that a very high per centage of cases of incipient tuberculosis will react to the subcutaneous administration of tuberculin with the proper dose administered. To attempt to give a list of experiments and the names of the workers along this line would require a whole newspaper. I take the liberty to make this statement from the experimental evidence that has been published since the discovery of tuberculin by Koch. As has been mentioned elsewhere in this paper, the advanced cases of tuberculosis give very varying reactions. I think much of the difference in results claimed to have been obtained by different workers in this field are largely due to men who are over desirous of winning popularity through the journals (perhaps some of them through the daily papers), and in order to accomplish this, they must write on something. Since the tuberculin reaction has been quite popular for the last two or three years, they of course make an attempt. As a result of the over-enthusiastic attempts, it will no doubt be some time before the profession is in unity on this method of diagnosis of tuberculosis. The precutaneous, the inhalations, the administration by the mouth, and the sero-diagnosis, the cytodiagnosis and the x-ray diagnosis, I will not refer to.

Of the several methods of applying the tests, I believe the cutaneous is the only one unattended with danger. Several Calmette reaction cases have been reported with complete loss of an eye. The subcutaneous method has also been attended with some bad results. This I think, is due to a lack of knowledge of the proper dosage and unwise selection of the patient. Of the three methods, I believe the subcutaneous requires the most experience to be able to successfully handle a case, but I think it is the most reliable.